Research Today

VOLUME 8, ISSUE 1

JANUARY 2022

Published by: Chief Scientist's Office
59 MDW/ST
(210) 292-2097
(DSN 554)

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59th Medical Wing Science and Technology (ST) Diagnostics and Therapeutic Research Program

With the COVID-19 pandemic continuing to threaten American lives, the Air Force 59th Medical Wing's Science and Technology (ST) Diagnostics and Therapeutic Research Program is actively responding to improve rapid diagnostics and accurate diagnosis of the infection for early intervention to improve military readiness. To accomplish this mission, we have set forth the following objectives: 1) Identifying rapid, accurate, field-deployable diagnostic platforms that can be used out in the field by warfighters and medics to quickly and accurately detect COVID-19 infection, 2) Comparing COVID-19 diagnostic platforms for accuracy and sensitivity to determine the optimal platforms to use and transition to a full 510k FDA approval, and 3) Expanding the approval of various sample sources and transport medias to be used for detection on certain diagnostic platforms to address the shortage of supplies such as nasopharyngeal swabs and viral transport media.

Biomeme Franklin three9 System
https://biomeme.com

Currently, we have three projects funded by the Defense Health Agency and the Air Force Small Business Initiative Research agency to address our three objectives. The work will be carried out at the Center for Advanced Molecular Detection (CAMD) laboratory. Our first project is evaluating the sensitivity and specificity of a novel field-deployable real-time PCR platform called the Biomeme Franklin three9 system for COVID-19 detection in collaboration with the biotech company Biomeme. The Biomeme platform includes rapid GO-strips which enable nucleic acid extraction from samples, reverse transcription and amplification of the COVID-19 spike and ORF1ab genes all in one cartridge under 60 minutes. The results are then read on a smartphone allowing for simple use out in the field. Current samples sources approved for testing on the Biomeme system include nasopharyngeal swabs, oropharyngeal swabs and nasal swabs.

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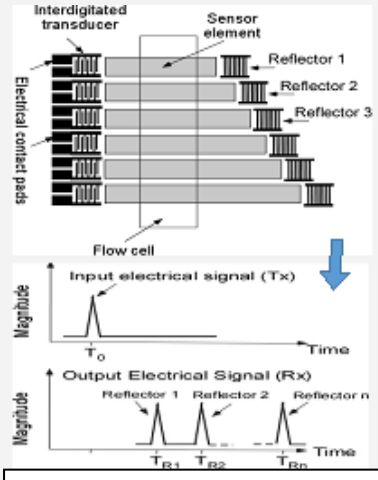
The second project is the development of a novel, field-deployable diagnostic platform for COVID-19 based on acoustic wave technology in collaboration with Aviana Molecular Technologies. This field-deployable system has several channels that not only allows multiplexing with different variations of the same molecule (e.g antibodies against the 'S' and 'N' proteins of COVID-19 to detect the virus), but can actually multiplex different variations of different molecules (e.g antibody against COVID-19 'S' protein to detect the virus in one channel, along with a COVID-19 'S' protein antigen in a separate channel to detect for antibodies against COVID-19 for immunity). This set-up allows for both COVID-19 virus detection and immunity all in the same cartridge and on the same device in less than 30 minutes with results being displayed via Bluetooth on a smartphone. Current samples sources being tested include nasopharyngeal swabs, oropharyngeal swabs, nasal swabs, saliva and whole blood samples obtained by a fingerprick.



Aviana Multiplexing Platform

Our final project is a comparison study looking at the Cepheid COVID-19 Xpress assay kit vs the Biofire Diagnostics Film array for COVID-19 detection. This project seeks to 1) compare both assays for sensitivity and specificity in various samples sources including nasopharyngeal swabs, nasal swabs, oropharyngeal swabs and saliva to determine which assay, if any, assay performs best. 2) Validate that these assays work equivalently well in approved sample sources (e.g nasopharyngeal swab) and unapproved sample sources (e.g saliva) to obtain approval for sample use expansion. 3) Lastly, this project will perform a comparison of standard viral transport media vs saline for swab-based samples with respect to sensitivity and specificity to determine if saline can be used as an alternative transport media to address supply issues.

Altogether, the successful completion of these projects and objectives will improve the methods for detection and diagnosis of COVID-19, and assist in addressing reagent supply shortages that are currently hindering COVID-19 response efforts. Importantly, the open, modular design of the novel diagnostic platforms in development can also be used for detection of other pathogens and injury/disease biomarkers, enabling these platforms to be permanent improvements to DoD capabilities that can extend beyond the COVID-19 pandemic. Such capabilities will improve military readiness, return-to-duty rates, and response strategies to future pandemics and infectious diseases occurring military conflicts.

59 MDW Investigator Takes 2nd Place at UT Health Military City USA Symposium Oct 20-21, 2021

Maj Tyler Davis, the Medical Director for the En Route Care Research Center within the 59MDW/ST Joint Austere Program attended and presented one of his projects "Association of hypocalcemia with clinical outcomes of combat casualties with TBI transported by Critical Care Air Transport Teams (CCATT)."

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A warm congratulations to Maj Davis as he was awarded 2nd Place in the Trainee Poster Presentations.

Maj Tyler Davis

The 2021 Military City USA Trauma Collaborative Research Conference was a regional, virtual conference that included sessions on oxygen delivery and shock management; hemorrhage and vascular dysfunction; metabolic failure and organ dysfunction; wound progression and infection; pain, sensory trauma, and mental status; and engineering solutions to enable combat casualty. The event also served as a forum to present clinical, translational, and basic science research that would have been presented at the 2021 Military Health Research System Research Symposium and other canceled trauma-related conferences due to the global health condition.

Association of Hypocalcemia with Clinical Outcomes of Combat Casualties with TBI Transported by Critical Care Air Transport Teams (CCATT)

ABSTRACT

Hypocalcemia at hospital presentation is associated with increased mortality in trauma patients with hemorrhagic shock. The 2019 updates to the Joint Trauma System Damage Control Resuscitation (DCR) Clinical Practice Guideline recommend calcium supplementation for ionized calcium (iCa) measurements <1.2 mmol/L. Ionized calcium goals for en route critical care (ERCC) following DCR are less defined, and the impact of in-flight hypocalcemia events among critically injured combat wounded is unknown. This study aimed to describe the association between hypocalcemia and mortality for combat wounded polytrauma patients transported by Critical Care Air Transport Teams (CCATT). We performed a secondary analysis of a retrospective cohort of patients with moderate to severe traumatic brain injury (TBI) transported by CCATT out of combat theater between January 2007 and May 2014. Additional inclusion criteria included polytrauma and at least one documented in-flight iCa measurement. We categorized exposures based on the minimum in-flight iCa measurement as severe hypocalcemia (iCa < 0.9 mmol/L), hypocalcemia (iCa 0.9 -1.11 mmol/L), and never hypocalcemic (iCa ≥ 1.12 mmol/L). The primary outcome measure was mortality. We calculated descriptive statistics and performed multivariate logistic regression to assess the association between hypocalcemia and mortality. We analyzed 190 subjects, with a median age of 24 years (interquartile range [IQR] 21 to 29 years) and 97.7% male gender. Explosive injuries (82.1%) and gunshot wounds (6.3%) were the most common mechanisms of injury. The median injury severity score was 34 (IQR 27 to 43). During the flight, 11.6% of patients had severe hypocalcemia, and 39.5% had hypocalcemia. Among patients with any hypocalcemia measurement in-flight (n=97), 41.2% had hypocalcemia on pre -flight iCa, 28.9% received blood products in-flight, and 23.7% received in-flight calcium supplementation. There was no significant difference in mortality between severe hypocalcemia (9.1%),

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hypocalcemia (5.3%), and never hypocalcemic (3.2%) patients even after controlling for pre-flight variables. In-flight hypocalcemia events were common among critically ill combat wounded polytrauma patients transported by CCATT but were not associated with differences in mortality.

59MDW En route Care Research Center: Informing Best Practices in Combat Casualty Care

The 59MDW/ST ECRC is busy with multiple on-going studies, dissemination of research findings, and seeking funding for future projects. Maj William Tyler Davis received 2nd place award for best poster at the 2021 Military City USA Conference for "Association of hypocalcemia with mortality of combat casualties with polytrauma transported by Critical Care Air Transport Teams." The results of this study have been submitted for publication in the Military Medicine journal. Davis WT, Ng PC, Cutright JE, Savell SC, Arana AA, McCarvel B, Maddry JK. Descriptive Analysis of Coronavirus Disease 2019 Air Medical Evacuations by Critical Care Air Transport Teams. Air Med J. 2021 Sep 27: doi: 10.1016/j.amj.2021.09.005 [Epub ahead of print]

Other Manuscript efforts:

*Ng PC, Arana AA, Savell SC, Davis WT, Perez CA, Bebarta VS, Maddry JK. Evacuation Strategies for U.S. Casualties with Traumatic Brain Injury. Mil Med. In press. Review/Revision in process.

*Davis WT, Ng PC, Medellin K, Cutright J, Arana AA, Strilka R, Sorensen D, Maddry JK. Association of hypocalcemia with mortality of combat casualties with polytrauma transported by Critical Care Air Transport Teams - submitted to Mil Med October 2021.

*Davis WT, Cheney M, Trueblood W, Runyon S, Cruz I, Clemons M, Strilka R. En route critical care evacuations from rarely utilized partner medical treatment facilities: A case series with lessons learned – submitted to Mil Med November 2021.

Recent Grant awards: Awarded funding for 14 DHA J-9 studies between ECRC, CRESTT and UCD.

Recent Grant Submissions:

*FY22 SA 711th - Reliability of Continuous Noninvasive Hemoglobin Monitoring during Air Transport: A Proof of Concept

*FY22 BAA USAMRDC - Critically Ill Patients with Disease and Nonbattle Injuries Evacuated by Critical Care Air Transport Teams

59MDW Science & Technology CIRS Sequencing and Bioinformatics Core Laboratory

The 59MDW/STC Clinical Investigations and Research Support (CIRS) Molecular Department has been serving 59 MDW investigators for over 10 years. During this period the selection, development, and validation of bioinformatic methods to process, evaluate, and interpret enormous amounts of next generation sequencing data has become increasingly urgent. The current pandemic further highlighted the importance of near real-time bioinformatic analysis of whole genome data for clinically relevant pathogens, such as SARS-CoV-2, as well as much more complex organisms including humans. In response to this research need, the CIRS Molecular Department has evolved capabilities and is now the CIRS Sequencing

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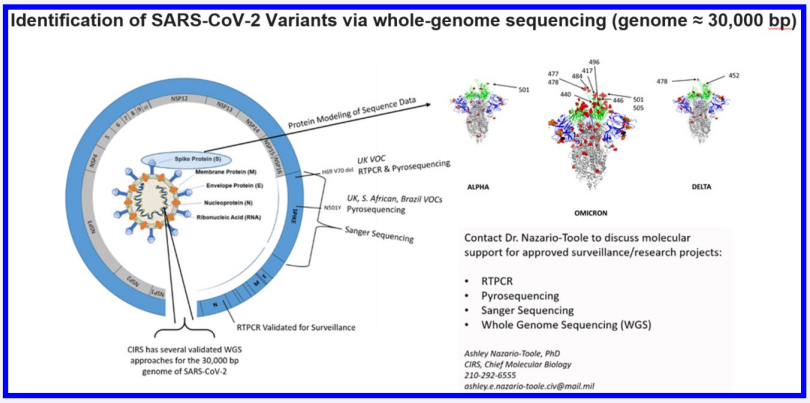
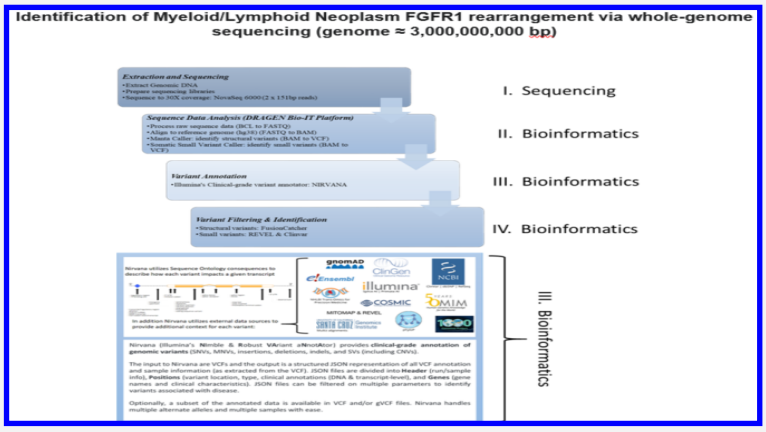
and Bioinformatics Core Laboratory. Dr Nazario-Toole, who on 5 Dec 2021 accepted the role as the lead scientist for this new and improved core laboratory service, is leading the work being done behind the scenes to ensure JBSA investigators have the tools they need to conduct cutting edge research. DHA researchers here at JBSA now have sequencing & bioinformatics support for Genomic, Transcriptomic, Epigenomic & Metagenomic Sequencing for just about any research need. In early spring of 2022 this will include Single-cell Sequencing options as well. Two recent examples of ongoing research being conducted by investigators are illustrated below; the first is for a 30,000 base pair genome and the second is for a genome that is 100,000 times larger and arguably as many times as complex, the human genome. As of Dec 2022 the CIRS Sequencing and Bioinformatics Core Laboratory has sequenced over 500 positive SARS-CoV-2 specimens; identifying variants in real-time as they appear here in the JBSA area. This work is conducted under an IRB approved protocol to sequence excess clinical specimens, and the data is reported to local public health authorities as well as the Armed Forces Health Surveillance Center.



The below figure outlines the sequencing and bioinformatics analysis steps utilized to provide whole genome data to a JBSA active duty Pathology Resident conducting an IRB approved case study on bone marrow and lymph node biopsies. Note, three of the four steps required to produce a report for the investigator rely solely on Bioinformatic analysis, highlighting the fact that Bioinformatics is required for meaningful interpretation of data covering 3 billion base pairs. Ultimately, the whole genome sequencing conducted at CIRS confirmed an in-frame fusion between two genes (FGFR1 rearrangement), identified a pathogenic frameshift mutation in another gene as well as two other missense variants relevant to the neoplasm. As a core support laboratory, all samples and data belong to the submitting Principle investigator (PI), which in this case is Major Holmes. The PI and others on the research team were able to utilize the whole genome data from CIRS to enhance the understanding of this particular type of neoplasm as well improve the quality of the publication currently being submitted to a Precision Oncology Journal. This is just one example of how a JBSA investigator can utilize the equipment and expertise available at CIRS to support their research needs.



SAN ANTONIO MILITARY MEDICAL INDUSTRY DAY III

April 19, 2022 | Henry B. Gonzalez Convention Center |8:00 AM - 4:30 PM

Join leaders from military medicine, industry, academia, and other organizations to exchange ideas and foster collaborations focused on R&D and commercialization. Topics will include addressing military medical needs, pitching ideas, and securing funding. This free in-person event is being co-hosted by the San Antonio Economic Development Corporation and VelocityTX. There will be three monthly hybrid mini-symposia/webinars leading up to the in-person event, with informational/instructional presentations in the morning and opportunities to discuss ideas (topic-based) with panels of subject matter experts during the afternoon of the event. Lunch will be provided for those who register for the event (see link below).

SA MMID Website: http://sanantonio.gov/EDD/Media-Resource-Center/Military-Medical-Industry-Day-III

Questions: EDDInfo@sanantonio.gov

Submit Topic Ideas (for pm session): corey@saedc.org

Vendor Display Info: Ruben.Davila@sanantonio.gov

SAVE THE DATE!

SUBMIT TOPIC IDEAS ASAP!

Science and Technology Contact Information

Our Vision

Grow Medical Leaders, Drive Innovations in Patient Centered Care and Readiness

Our Mission

Conduct clinical studies and translational research and apply knowledge gained to enhance performance, protect the force, and advance medical care and capabilities

Points of Contact

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Public site: http://www.59mdw.af.mil/Units/ChiefScientist-ST.aspx

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